Citalopram reduced depressive symptoms in coronary artery disease with depression

Lespérance F, Frasure-Smith N, Koszycki D, et al. **Effects of citalopram and interpersonal psychotherapy on depression in patients with coronary artery disease: the Canadian Cardiac Randomized Evaluation of Antidepressant and Psychotherapy Efficacy (CREATE) trial.** JAMA. 2007;297:367-79.

Clinical impact ratings: Mental Health ★★★★★★★ GIM/FP/GP ★★★★★★☆ Cardiology ★★★★★★☆

QUESTION

In patients with coronary artery disease (CAD) and major depression, how effective are citalopram and interpersonal psychotherapy (IPT) in reducing depressive symptoms?

METHODS

Design: Randomized controlled 2×2 factorial trial (Canadian Cardiac Randomized Evaluation of Antidepressant and Psychotherapy Efficacy [CREATE]).

Allocation: Concealed.*

Blinding: Blinded (therapists, patients, site psychiatrists, telephone raters, outcome assessors, coordinating center personnel, and adverse event committee).*

Follow-up period: 12 weeks.

Setting: 9 academic centers in Canada.

Patients: 284 patients ≥ 18 years of age (mean age 58 y, 75% men) with major depression lasting > 4 weeks; a score ≥ 20 on the 24-item Hamilton Depression Rating Scale (HAM-D); and established, stable CAD. Exclusion criteria included bipolar disorder or major depression with psychotic features; suicide risk; current use of antidepressants, lithium, anticonvulsants, or psychotherapy; previous lack of response or early termination of depression medications; planned coronary artery bypass graft surgery; and severe angina.

Intervention: Patients had 2 separate randomizations: first to clinical management (CM) plus IPT (n = 142) or CM alone (n = 142) and then to CM plus IPT and citalopram (n = 67), CM plus IPT and placebo (n = 75), CM and citalopram (n = 75), or CM and placebo (n = 76). Citalopram was titrated to 20 mg/d and could be increased to 40 mg/d.

Outcomes: Change on the HAM-D scale and the Beck Depression Inventory II (BDI-II). Exploratory outcomes included scores on the Inventory of Depressive Severity (IDS), Functional Performance Inventory (FPI), and the Interpersonal Relationships Inventory (IPRI).

Patient follow-up: 94% (intention-to-treat analysis).

MAIN RESULTS

Citalopram improved the HAM-D and BDI-II scores more than placebo (Table). No difference was seen between IPT plus CM and CM alone (Table). Citalopram also showed greater improvement in scores on the IDS (effect size 0.37) and IPRI (effect size 0.33) and a borderline improvement on the FPI (effect size 0.21). IPT and CM did not differ for those measures.

CONCLUSION

In patients with coronary artery disease and major depression, citalopram reduced depressive symptoms more than placebo, and interpersonal psychotherapy did not differ from clinical management.

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*See Glossary.

Citalopram vs placebo, and interpersonal therapy (IPT) vs clinical management (CM) for coronary artery disease with depression at 12 weeks†

Outcomes	Comparisons	Mean reductions in scores	Between-group difference
24-item Hamilton Depression Rating Scale	Citalopram vs placebo	14.9 vs 11.6	3.33 (96.7% CI 0.80 to 5.85)
	IPT vs CM	12.1 vs 14.4	−2.26 (96.7% CI −4.78 to 0.27
Beck Depression Inventory II	Citalopram vs placebo	14.7 vs 11.1	3.61 (98.3% CI 0.58 to 6.64)
	IPT vs CM	13.5 vs 12.4	1.13 (98.3% CI −1.90 to 4.16)

†CI defined in Glossary.

COMMENTARY

The results from CREATE are provocative, timely, and important. The study is substantial in scope, amply powered, and impeccably designed and executed. As is often the case, even the best studies answer some questions and raise new ones.

CREATE (especially when added to extant literature) makes it clear that effective treatment options exist for depressed cardiac patients. Depending on urgency, affordability, and patient preference, selective serotonin reuptake inhibitors (SSRIs) or psychological support can be offered, with SSRIs providing a quicker response and larger effect after 4 months. It was quite surprising that IPT did not fare better than clinical management (offered by the same trained psychotherapists). Given that both reduced depression, it suggests that 6 hours of professional psychological support (in 12 half-hour periods) is an active rather than inert intervention. As for practice recommendations, depression in cardiac patients is treatable without compromising safety; hence, good reason exists to make such treatment routine practice.

Consistent evidence shows that depression has a poor prognosis, but no convincing evidence exists that treating depression will also reduce mortality, irrespective of the mode of treatment. Long-term follow-up of CREATE will not provide additional information because after participation in the trial, all patients received usual care. Extended follow-up in future trials is needed; this is especially important because pharmacologic treatment leads to swifter initial improvement in depression, but cognitive behavioral therapy holds more promise for maintaining gains (1). Although CREATE clearly speaks against routine use of IPT, it adds limited insights to the larger, nagging questions of which psychological intervention to use, who will administer it, and for how long. Meta-analysis suggests that psychological treatment of distress reduces mortality in cardiac patients only if it is actually successful (2), thus arguing against offering the same fixed number of treatment sessions or the same type of approach to all patients. At the least, this insight calls for repeated assessments of distress and depression as cardiac patients complete their rehabilitation program.

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